

Delaware Physical Exercise and Activity for Knee osteoarthritis (PEAK)

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Affected Section(s)	Summary of Revisions Made	Rationale

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STATEMENT OF COMPLIANCE

The trial will be conducted in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP), applicable United States (US) Code of Federal Regulations (CFR), and the Rheumatology Research Foundation Terms and Conditions of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

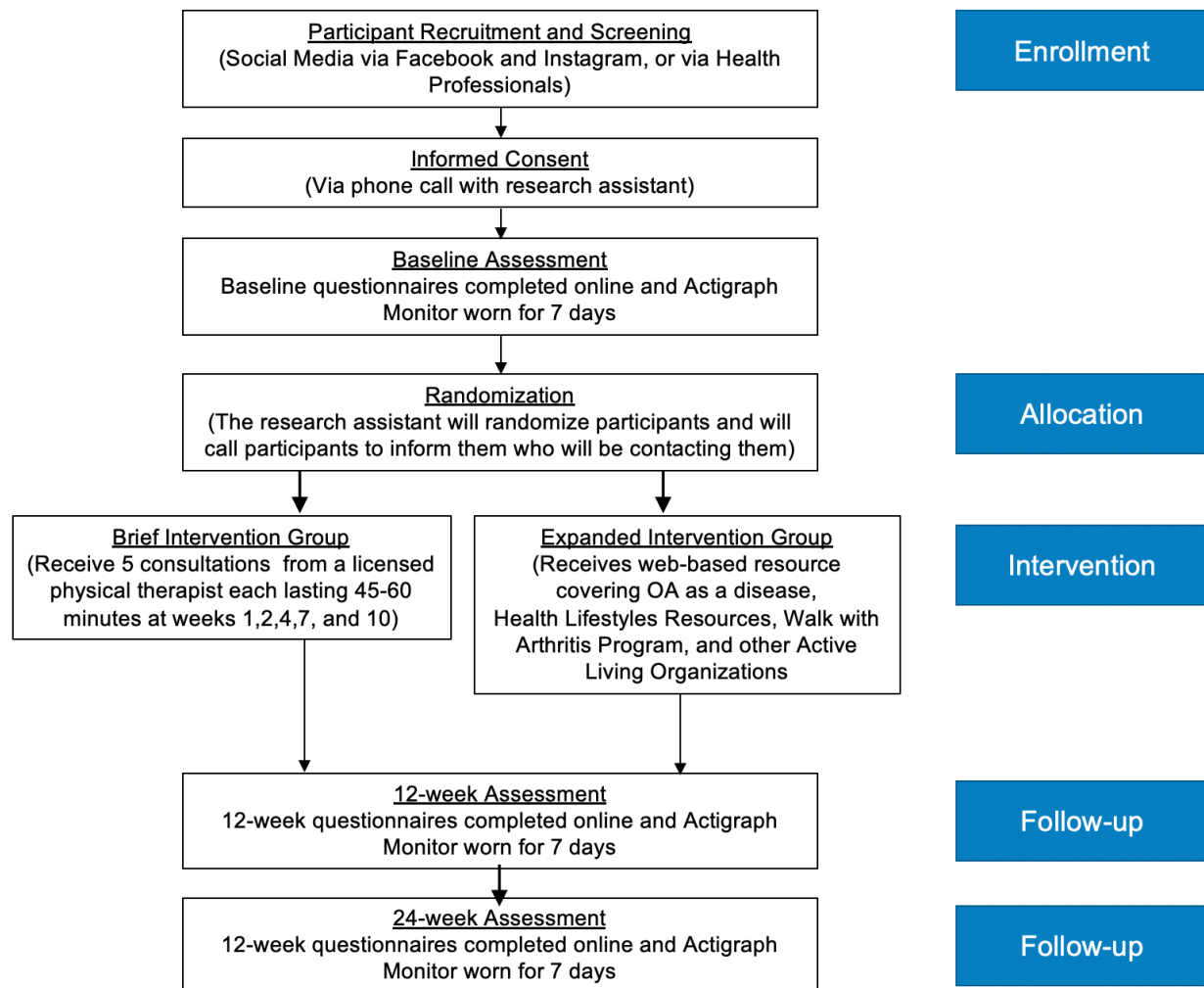
1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Delaware Physical Exercise and Activity for Knee osteoarthritis (PEAK)
Study Description:	We will conduct a randomized controlled trial of 100 adults with knee OA receiving a brief- or expanded-exercise and physical activity intervention. We hypothesize those receiving the expanded intervention will increase physical activity over 12 weeks.
Objectives:	The objective of this proposal is to compare a brief versus expanded exercise and physical activity intervention, both delivered online, to increase physical activity in adults with knee osteoarthritis (OA).
Endpoints:	Primary Endpoint: Change in moderate-to-vigorous intensity physical activity (MVPA) from baseline to 12 weeks. Secondary Endpoints: Changes in health beliefs and self-efficacy from baseline to 12 weeks.
Study Population:	100 adults with a clinical diagnosis of knee OA (≥ 45 years with activity related knee joint pain) residing in the continental United States, and participate in < 60 minutes/week in exercise
Phase:	2
Description of Sites/Facilities Enrolling Participants:	The trial will take place virtually, and be based from the University of Delaware.
Description of Study Intervention:	The Expanded intervention will include 5 consultation sessions with a licensed Physical Therapist over video conferencing with each session lasting between 30 to 45 minutes to set goals for strengthening exercises and physical activity. The Brief intervention will include a web-based resources for strengthening exercises and physical activity.

Study Duration: 24 months
Participant Duration: 24 weeks

1.2 SCHEMA



Schedule of Activities (SoA)

24-week Data Collection Completed Day 206 -7 Days/+28 Days												
Call 4 (23 week contact) Day 182 -0 Days/+7Days						X						
12-week Data Collection Completed Day 112, -7 Days/+28 Days							X					
Call 3 (11-week contact) Day 98, -0 Days/+7Days						X						
Expanded Intervention ^b , Day 21												
Brief Intervention ^a , Day 21												
Call 2 (Randomization), Day 14, -0 Days/+7Days												
Baseline Data Collection Completed Day 14, -7 Days/+7Days				X	X	X	X	X	X	X	X	X
Enrollment, Day 0			X									
Call 1 (Eligibility)		X										
Online Screening	X											
Procedures	Screening Form (4-item questionnaire online)											
	Verbal Eligibility Form		X									
	Informed Consent			X								
	General Information (Demographics), Emergency and Participant Contact				X							
	IPAQ				X							
	Actigraph, ActivPAL				X						X	
Provider Form				X								
OA Information Form				X								
Charlson Comorbidity Index				X								
Visual Analogue Scale				X								X

	24-week Data Collection Completed Day 206 -7 Days/+28 Days	X	X	X						
	Call 4 (23 week contact) Day 182 -0 Days/+7Days							X		
	12-week Data Collection Completed Day 112, -7 Days/+28 Days	X	X	X						
	Call 3 (11-week contact) Day 98, -0 Days/+7Days							X		
	Expanded Intervention ^b , Day 21							X		
	Brief Intervention ^a , Day 21							X	X	
	Call 2 (Randomization), Day 14, -0 Days/+7Days					X		X		
	Baseline Data Collection Completed Day 14, -7 Days/+7Days	X	X	X	X					
	Enrollment, Day 0									
	Call 1 (Eligibility)									
	Online Screening									
Procedures										
Knee Injury and OA Outcome Score										
Treatment Beliefs of Physical Therapy										
Treatment Beliefs of Physical Exercise										
General Beliefs about Knee OA										
Self-Efficacy for Exercise										
Treatment Expectations Question										
Randomization										
Adverse event review and evaluation										
Email link for the Brief exercise and physical activity intervention ^a										
Brief Intervention Questions ^a										

2 INTRODUCTION

2.1 STUDY RATIONALE

Knee Osteoarthritis (OA) is a serious disease. In 2010, OA moved up from 15th to 11th in rankings for global burden of disease,¹⁹ and the most common weight-bearing joint affected by OA is the knee.²⁰ More than 15 million Americans currently have symptomatic knee OA.²¹ The estimated annual cost to treat knee OA is \$27 billion,²² which is similar to the cost to treat stroke (~\$34 billion²³). The incidence of knee OA is expected to increase with the aging and obese US population.²⁴ Walking difficulty is the primary functional limitation in people with knee OA that, in turn, makes OA the leading cause of disability among older adults.²⁵ Not only is walking difficulty related to disability, but it is also associated with a 55% higher risk of premature death.^{10,26} Without a cure, treatment for knee OA focuses primarily on managing pain and reducing disability.

Treatment guidelines for knee OA champion the use of supervised exercise. The recently released 2019 ACR/Arthritis Foundation guidelines for the treatment of OA strongly support the use of supervised exercise.¹ These recommendations are consistent with those of the Osteoarthritis Research Society International (OARSI), which promote exercise, self-management, and education.² Both guidelines (ACR and OARSI) come from the robust and pervasive research findings that exercise reduces pain and improves physical function in adults with knee OA.¹⁰

Few adults with knee OA try supervised exercise to manage their OA. For example, less than 10% of adults with knee OA exercise regularly,^{3,4} and only one-in-ten patients are seen for supervised exercise 5 years before a knee replacement.⁵ Health claims data show a similar trend, with a doubling in the prescription of opioids and a 50% reduction in referrals for Physical Therapy (PT) in the past decade.⁹ Hence, few adults with knee OA are utilizing physical activity and/or supervised exercise to address their symptoms of knee OA.

The objective of this proposal is to examine the efficacy of Delaware PEAK to increase physical activity in adults with knee OA compared to a control group receiving web-based resources about knee OA and exercise. The rationale for our study is that there is a need to examine whether Delaware PEAK can directly target the mismatch between OA recommendations and practice patterns. Our central hypothesis is that Delaware PEAK will increase physical activity and will increase the belief that exercise is helpful and not harmful, compared with a control group receiving web-based OA treatment resources. Successful completion of this proposal will provide the evidence necessary to scale up this low-cost intervention, with the goal of increasing the number of adults who use exercise to manage their knee OA and thus reducing the burden of disease.

2.2 BACKGROUND

We investigated why so few adults with knee OA engage in exercise. Our research group conducted a series of qualitative studies to understand reasons for the mismatch between guidelines and practice. We interviewed adults with knee OA in the community,^{6,7} and primary care physicians who commonly treat knee OA.¹¹ Among patients, we found there to be misunderstanding about OA as a disease, little knowledge of the benefits of physical activity,

and low confidence or self-efficacy for exercise.^{6,7} Patients in our qualitative study stated they thought OA meant you were ‘bone on bone’ and “[supervised exercise] can’t help bone on bone”. Another patient expressed little hope for exercise to be helpful, stating, “Surgery is the only thing that really helps”.⁶ Among primary care physicians, we discovered that exercise, the main treatment for OA, was often not perceived as a “real” medical treatment and prescribing exercise was outside of most physician’s scope of practice. These findings are consistent with other studies that show healthcare providers are reluctant to recommend exercise. For example, less than 2/3rds of patients are told to exercise by licensed healthcare professionals¹². This is a major problem, given that receiving a clinical recommendation is the single most important factor associated with exercising regularly.^{13,14} *These findings highlight the critical need to ‘myth-bust’ misconceptions about disease and exercise for OA, and implement exercise recommendations for OA into a step-by-step standardized program for ease of clinician delivery.*

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

- **Brief Exercise and Physical Activity Intervention**

In response to initiating exercise, there is a minimal risk of an adverse medical event, i.e., an unexpected event such as ill health, physical harm, or death. There are no known risks associated with receiving education on web-based resources for strengthening and physical activity. Should the study participant initiate exercise, there is risk of muscular soreness, fluctuating knee pain and/or swelling related to knee OA, and fatigue during or following exercise. Should the participant start the ‘Walk with Ease’ program, there is risk of a mild, temporary increase in knee pain.

- **Expanded Exercise and Physical Activity Intervention**

In response to initiating exercise, there is a minimal risk of an adverse medical event, i.e., an unexpected event such as ill health, physical harm, or death. Much more common are risks associated with participation typically found during a physical therapy intervention, e.g. risk of soreness from exercises designed to increase muscle strength or length, fluctuating knee pain and/or swelling related to knee OA, and fatigue during or following the treatment. There is a minimal risk of a loss of balance during exercises that involve standing or single limb stance. There is a minimal risk for starting a supervised physical activity program, including a mild temporary increase in knee pain.

- **activPAL 4 Monitor**

Risks include skin irritation or skin reaction to the nitrile flexible sleeve and/or Tegaderm medical dressing that are used to waterproof and adhere the monitor to the skin, respectively.

- **Actigraph GT3X Monitor**

There are no known risks associated with wearing the Actigraph GT3X monitor.

- **Questionnaires**

Some of the questionnaires require the respondent to consider pain, how this pain affects daily tasks, and other health problems. It is possible that some people could find these questions difficult emotionally, although we have not found this to be a problem in other similar studies.

- **Data Breach**

There is a possibility of a breach of confidentiality if data or identifying information should accidentally be viewed, though this is very unlikely.

2.3.2 KNOWN POTENTIAL BENEFITS

Participants in our study may experience relief of OA symptoms such as pain or stiffness, and an overall increase in lower body strength. The participant may also improve their physical activity, which is associated with improved cardiovascular health, and improved quality of life.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

- **Brief Exercise and Physical Activity group**

Part of the education will review web-based resources that detail common side effects of initiating an exercise and physical activity program, and when one should seek help. As with the expanded group, study inclusion criteria requires pre-participation screening from Stage 1 of the APSS questionnaire, which classifies adults into low-risk of adverse events, or moderate to high-risk of adverse events from initiating exercise. We require study participants who have moderate to high-risk of adverse events to obtain medical clearance prior to starting the study thereby mitigating adverse medical events that emerge in response to initiating exercise. As well, we are excluding study subjects who report any unstable/uncontrolled cardiovascular condition.

- **Expanded Exercise and Physical Activity group**

Study inclusion criteria requires pre-participation screening from Stage 1 of the APSS questionnaire, which classifies adults into low-risk of adverse events, or moderate to high-risk of adverse events from initiating exercise. We require study participants who have moderate to high-risk of adverse events, to obtain medical clearance prior to starting the study thereby mitigating adverse medical events that emerge in response to initiating exercise. As well, we are excluding study subjects who report any unstable/uncontrolled cardiovascular condition. As this intervention is delivered remotely, we have planned for response in case of an unexpected need for face-to-face help. We will begin each consultation with the study subject providing a phone number of a friend or family member who is in the closest physical proximity to him/her and can be contacted in case of emergency. Also, the study subject will provide his/her physical location (address) where he/she will be receiving the intervention. A physical therapist will provide a tailored exercise and physical activity program that will be scaled to the patient's ability to increase strength, but not beyond his/her abilities. Specifically, a physical therapist will assign exercises according to his/her abilities and will provide rest breaks as needed to minimize soreness and fatigue.

- **activPAL 4 Monitor**

To minimize the risk of skin irritation, the participant can periodically remove the activPAL 4 monitor from their right thigh and switch it to their left thigh.

- **Questionnaires**

To minimize the risk of an emotional response, we will offer participants the option to contact the research team and ask any questions they may have.

- **Data Breach**

To minimize the risk of breach of confidentiality, all participant data will be stored in secure, locked cabinets and/or on a secure server (including REDCap).

Given these attempts to minimize adverse events from participation with the potential benefit of the intervention, the information to be gained from our study outweighs the risk of participation.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
To evaluate the efficacy of a remotely delivered physical activity and exercise intervention to increase physical activity compared to a brief intervention consisting of web-based resources for the managing OA.	Change in moderate-to-vigorous intensity physical activity (MVPA) from baseline to 12-week measured with an Actigraph GT3x monitor	<i>Physical activity is our primary study outcome, and MVPA is an intensity of physical activity linked to many health benefits, especially for adults with knee OA</i>
Secondary		
To examine changes in health beliefs and self-efficacy	<u>Health Beliefs:</u> Change in the Treatment Beliefs of OA Physical Therapy and Physical activity scales from baseline to 12 weeks. <u>Self Efficacy:</u> Change in the Self Efficacy for Exercise scale from baseline to 12 weeks.	<i>PEAK is hypothesized to improve health beliefs and self efficacy. Hence, we will measure change in these outcomes.</i>
To evaluate the efficacy of a remotely delivered physical activity and exercise intervention to increase physical activity compared to a brief intervention consisting of web-based resources for the managing OA.	Change in moderate-to-vigorous intensity physical activity (MVPA) from baseline to 24 weeks measured with an Actigraph GT3x monitor	<i>We additionally will examine changes in MVPA over 24 weeks.</i>
Tertiary/Exploratory		

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
N/A	N/A	N/A

4 STUDY DESIGN

4.1 OVERALL DESIGN

Our central hypothesis is that the remotely delivered physical activity and exercise intervention, which we call Delaware Physical Exercise and Activity for Knee osteoarthritis (PEAK), will increase physical activity, will increase the belief that exercise is helpful and not harmful, and will increase self-efficacy compared with a control group receiving web-based OA treatment resources.

To test this hypothesis, we will conduct a Phase 2 randomized controlled trial assigning subjects meeting study criteria into either the remotely delivered physical activity and exercise intervention, i.e., the expanded intervention, or the web-based OA treatment resources, i.e., the brief intervention. The study will be based from the University of Delaware, but we will recruit study subjects within the continental United States.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

We selected a two-arm randomized controlled design study in order to minimize potential confounding from known and unknown sources. We selected a control group that provides web-based resources for OA management, including pain management, exercises, and physical activity, which we call the brief intervention, since these resources are the standard-of-care for adults with knee OA. We chose a superiority design since we hypothesized the expanded intervention would result in greater improvement in physical activity compared with the brief intervention.

Treatment guidelines for knee OA champion the use of supervised exercise. The recently released 2019 ACR/Arthritis Foundation guidelines for the treatment of OA strongly support the use of supervised exercise.¹ These recommendations are consistent with those of the Osteoarthritis Research Society International (OARSI), which promote exercise, self-management, and education.² Both guidelines (ACR and OARSI) come from the robust and pervasive research findings that exercise reduces pain and improves physical function in adults with knee OA.¹⁰

Few adults with knee OA try supervised exercise to manage their OA. For example, less than 10% of adults with knee OA exercise regularly,^{3,4} and only one-in-ten patients are seen for supervised exercise 5 years before a knee replacement.⁵ Health claims data show a similar trend, with a doubling in the prescription of opioids and a 50% reduction in referrals for Physical Therapy (PT) in the past decade.⁹ Hence, few adults with knee OA are utilizing physical activity and/or supervised exercise to address their symptoms of knee OA.

We investigated why so few adults with knee OA engage in exercise. Our research group conducted a series of qualitative studies to understand reasons for the mismatch between guidelines and practice. We interviewed adults with knee OA in the community,^{6,7} and primary care physicians who commonly treat knee OA.¹¹ Among patients, we found there to be misunderstanding about OA as a disease, little knowledge of the benefits of physical activity, and low confidence or self-efficacy for exercise.^{6,7} Patients in our qualitative study stated they thought OA meant you were ‘bone on bone’ and “[supervised exercise] can’t help bone on bone”. Another patient expressed little hope for exercise to be helpful, stating, “Surgery is the only thing that really helps”.⁶ Among primary care physicians, we discovered that exercise, the main treatment for OA, was often not perceived as a “real” medical treatment and prescribing exercise was outside of most physician’s scope of practice. These findings are consistent with other studies that show healthcare providers are reluctant to recommend exercise. For example, less than 2/3rds of patients are told to exercise by licensed healthcare professionals¹². This is a major problem, given that receiving a clinical recommendation is the single most important factor associated with exercising regularly.^{13,14} *These findings highlight the critical need to ‘myth-bust’ misconceptions about disease and exercise for OA, and implement exercise recommendations for OA into a step-by-step standardized program for ease of clinician delivery.*

4.3 JUSTIFICATION FOR DOSE

A previous well-powered randomized controlled trial found an early version of PEAK using a similar number of consultations, but delivered via a telephone-based PT intervention (no video) to increase physical function as measured by the Western Ontario and McMaster Universities Arthritis Index (WOMAC) compared with a control group receiving a nurse-managed information session which is typical for usual care.⁸ *Delaware* PEAK is also supported by a previous study demonstrating clinically important improvements in pain and physical functioning following an Internet-delivered, Physical Therapist-prescribed home exercise and pain-coping skills training for adults with chronic knee pain, when compared with a control group receiving internet-based educational material.¹⁶

4.4 END OF STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed all phases of the study including the last visit or the last scheduled procedure shown in the Schedule of Activities (SoA), Section 1.3.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Provision of signed and dated informed consent form
2. ≥ 45 years of age,
3. Resides in the contiguous United States

4. Available for the duration of the intervention portion of the study (12 weeks) and willing to wear physical activity monitors
5. Looking to move more, i.e., be more active.
6. Knee OA diagnosis by the NICE criteria
7. Comfortable participating in a program delivered in English
8. Is able to safely participate in moderate-intensity exercise as determined by a pre-exercise screen questionnaire,²⁹
9. Has either a smartphone or a laptop/desktop computer with an internet connection.
10. Has a working email address.

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Regularly exercise for more than 60 minutes/week.
2. Has a scheduled knee or hip joint replacement
3. Has had physical therapy for knee OA in the past 6 months
4. Participated in a strength training program for the lower extremities in the past 6 months

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in the clinical trial but are not subsequently randomly assigned to the study intervention or entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

Individuals who do not meet the criteria for participation in this trial (screen failure) because of the following reasons may be rescreened after medical clearance from a licensed physician is obtained.

Fall in the past 12 months that resulted in an injury
 House-bound due to immobility in the past 12 months
 Has a heart condition or stroke
 Experience unexplained pains or discomfort in your chest at rest or during physical activity/exercise
 Feel faint, dizzy, or lose balance during physical activity/exercise
 Asthma attack requiring immediate medical attention at any time over the last 12 months
 Trouble controlling your blood sugar (glucose) in the last 3 months
 Presence of any other conditions that may require special consideration for exercise

Rescreened participants should be assigned the same participant number as for the initial screening.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

We will utilize two sources to recruit study subjects.

- The first is from health professionals. We have agreements from two major providers of care for adults with knee OA. The first is Delaware Orthopaedics Specialists (DOS). DOS treats 2000+ adults/year with knee OA. We have a strong working scientific and clinical relationship with DOS. We are currently conducting a clinical trial with knee injections in partnership with DOS that is foundation funded, and the Physical Therapy Clinic at UD receives an average of 10 to 12 referrals per month of patients knee OA from DOS. The second is Colorado Joint Replacement. This group treats 1000+ adults/year with knee OA. Dr. Brad Bley, a sports medicine physician at DOS, and Dr. Jason Jennings, an orthopaedic surgeon at Colorado Joint Replacement, have agreed to refer patients to our study. Both have included letters of support which can be found in the Appendix.
- The second is online via social media (SM). We will recruit study subjects from Facebook (FB) and Instagram (IG). The Physical Activity Lab has accounts with each SM provider, which we will use to advertise our study. Such recruitment methods have been successful within other laboratories in the Department of Physical Therapy. For example, the Tendon Lab recruited 65 subjects from FB. We have an active membership in several different arthritis support groups on FB.

Our target study sample will include 100 adults (50% women), and include 15% adults who are African American, and 20% who are Hispanic. Subjects will be at least 45 years of age. We anticipate screening 200 adults (50% women, 15% African American, and 20% Hispanic) in order to reach our target enrollment. We will recruit and enroll approximately 5 to 6 study subjects/month. We will enroll study subjects within the continental US. Retainment to facilitate subjects to successfully complete the study will occur through a \$50 financial incentive.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

Expanded Intervention Description:

Consultations 1-5 will take place approximately at study week 1, 2, 4, 7, and 10, respectively.

- **Pre-consultation survey:** Study participants are invited to complete [a pre-consultation survey](#) which asks about the patient's health and disease history, current pain, levels of physical activity, and personal goals.
- **Consultation 1 (60 minutes):** The initial consultation starts with a 5-minute introduction and expectation setting. The aims of the Delaware PEAK program are outlined and participants are oriented to resources (online, exercise bands, and Fitbit monitor) to help self-manage their knee OA. This is followed by a 10-minute assessment where goals the patient set as part of the pre-consultation survey are reviewed, and the patient's understanding of OA and the role of PT is ascertained, so misconceptions can be quickly corrected. Functional tasks, such as walking, stair climbing, and squatting are observed.

A 10-minute session on Education takes place next which orients the patient to the [Osteoarthritis Information booklet](#), which provides an introduction to the strengthening exercises and physical activity plan. The Physical Therapist is encouraged to ensure the patient understands the benefits of exercise and physical activity before prescribing a program. A 15-minute session is devoted to prescribing strengthening exercises, which are based on what the patient can manage. Together with the study subject, the [Exercise Booklet](#) is reviewed and one exercise each strengthening the knee extensors, hip abductors, and knee flexors is chosen. Patients are taught how to perform the exercises. This entails watching the patient perform each exercise and prescribing an exercise dosage. Ideally each exercise should feel “hard” to “very hard” to perform. Study subjects are taught how to record exercises in the [Knee Plan and Log Book](#), which will be used to track exercise adherence. Patients are also educated that pain/flare-ups may occur and are normal while performing strengthening exercises. Management strategies to address pain flares are discussed. 5 minutes are then spent on discussing the use of the Fitbit monitor to measure steps/day and an initial steps/day goal is set. Study participants will receive a Fitbit™ Inspire that is worn on the wrist and displays a daily step count. The PT will train the patient on the purpose of using a Fitbit™, how to use the device and sync it to a smart device such as an iPhone, and Android phone, or a tablet. The session will conclude with booking the next session.

- **Consultation 2 (45 minutes):** The second consultation begins with a 5-minute re-assessment to “check in” with the study subject in regards to changes in knee pain, success with performing strengthening exercises, and an opportunity to ask any questions from the first consultation. Next, a 10-minute session focusing on strengthening is initiated where progress is reviewed with the prescribed exercises. In particular, the Knee Plan and Log Book is reviewed, and if adherent, the study subject is congratulated. Reasons for non-adherence are discussed. If the subject is ready, the strengthening program is expanded to include ankle plantar flexor strengthening (calf strengthening), and another exercise of the subject’s choosing. As well, the existing exercises are progressed using techniques such as increasing resistance band and/or changing sets/repetitions. If the patient is not able to perform the task with the correct exercise technique the exercises are not progressed. As well, if the patient is experiencing increased pain and swelling lasting more than one day after their exercises, they should go back to a lower level, do fewer repetitions of their current level, or try an alternative exercise. A 5-minute education follows and focuses on making sure the study subject has sufficient knowledge and understanding of why a physical activity program can benefit their knee OA. Next, 10-minutes are spent on physical activity. The patient’s steps/day are reviewed, and a step goal is set. If a patient is walking >10,000 steps/day then it is ok to maintain that level of physical activity. A 10% increase is a rough guideline for how much to progress the steps/day goal. The physical therapist will agree on a personal (daily or weekly) physical activity plan with the study subject that will help them achieve the step goal and/or help them to increase the amount/intensity of physical activity they regularly undertake. Study subjects will be encouraged to think

about potential barriers to their physical activity plan, and think of potential strategies for overcoming barriers. The second session ends with booking the next consultation.

- **Consultation 3 (45 minutes):** The third consultation begins with a 5-minute re-assessment of knee pain, a self-assessment of adherence to strengthening to steps/day goals, an opportunity to ask questions and a visual re-assessment of functional activities. 10-15 minutes are then spent on progressing the strengthening exercises. This starts with a review of adherence from the “Knee Plan and Log Book”, and discussion of any reasons for non-adherence. Exercises are progressed in the same manner as described in consultation 2. 5 – 10 minutes are spent on the physical activity program, which follows the same format as consultation 2. 5 minutes are then spent on education discussing a chapter entitled “Understanding & Managing your Pain” from the OA book. The third consultation is concluded by scheduling the next session.
- **Consultation 4 (45 minutes):** The fourth consultation follows the same form as the 2nd and 3rd consultations with a re-assessment, and review and progression of the exercise and physical activity goals. Education for this consultation centers on weight loss, and is supported by a chapter entitled “Weight loss for OA” in the Osteoarthritis Information booklet.
- **Consultation 5 (45 minutes):** The fifth consultation starts with encouragement for study subjects to **continue with their strengthening exercise and physical activity plan into the future, i.e., after concluding the Delaware PEAK program.** The consultation then follows the same form as the 2nd, 3rd, and 4th consultations. A re-assessment is followed by a review and progression of the exercise and physical activity goals. Education in this final consultation focuses on expecting lapses in adhering to exercise and physical activity program from time to time- and that this is normal. The consultation ends with patients being encouraged to read “Success stories” from others from the Osteoarthritis Information booklet for ongoing motivation.

Brief Intervention Description:

- **(20 to 70+ minutes)** This group will receive real-world, online OA-related resources that are available to adults with knee OA, thereby formally providing resources common with existing care. We modeled the Brief Intervention group after that of a previous published large RCT.²⁷ Participants will receive a guided orientation to resources available online. The orientation will be given by a physical therapist via a pre-recorded video. The following resources will be discussed: 1) an overview of disease, 2) Health Lifestyle resources including Physical Activity and Weight Management, and 3) the Walk with Arthritis Program. Preparation/Handling/Storage/Accountability

6.1.2 ACQUISITION AND ACCOUNTABILITY

N/A

6.1.3 FORMULATION, APPEARANCE, PACKAGING, AND LABELING

N/A

6.1.4 PRODUCT STORAGE AND STABILITY

Describe storage and stability requirements (e.g., protection from light, temperature, humidity) for the
N/A

6.1.5 PREPARATION

N/A

6.2 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Randomization will be into one of the two intervention groups using block randomization with block sizes of 4. Block randomization will result in equal sample sizes throughout the study. Prior to the phone call, the study team will create a study-specific Google Account for each participant. The Brief Intervention group will use this account to access the Brief Intervention website and the Expanded Intervention group will use it to set up their Fitbit. While the participant is still on the phone, the research coordinator will again administer the Treatment Expectations Question.

Participants will not be blinded to group allocation, although they will be concealed from knowledge of the content of the other group. As well, participants will not be informed about the study hypotheses until the study is completed, at which time they will be provided a lay summary of findings. Research team members responsible for outcome data management will be blinded to group assignment. However, the treating physical therapist will not be blinded to group assignment, as they are delivering both interventions to ensure physical therapist-related factors such as personality, clinical practice experience, etc. are similar across groups and cannot confound results. As all outcomes are collected either through a physical activity monitor or online questionnaires, this study is thus considered assessor-blinded. Statistical analyses will be performed in a blinded manner.

6.3 STUDY INTERVENTION COMPLIANCE

Treatment fidelity will be assessed to determine if the Expanded Intervention was appropriately delivered. Each consultation session will be video-recorded and reviewed by a Research Assistant who will score the session on the following domains: Assessment, Strengthening Exercise, Physical Activity, Education, and Motivational Interviewing. Each domain will be assessed using a yes/no checklist and expressed as a percentage.

6.4 CONCOMITANT THERAPY

N/A

6.4.1 RESCUE MEDICINE

N/A

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

Should AEs in the intervention group exceed an OR of 3.0, 95%CI [2.5, 3.5], then the intervention will be temporarily paused to allow an investigation by the study team as to possible reasons for the increased risk of AEs. Should SAEs in the intervention group exceed an OR of 2.0, 95%CI [1.5, 2.5], then the intervention will be temporarily pause to allow an investigation by the study team as to possible reasons for the increased risk of SAEs.

If the intervention is temporarily paused, efforts will be made to continue follow-up of participants who discontinue the study intervention, but remain in the study for follow-up, especially for safety and efficacy study endpoints. Reasonable efforts must be made to undertake protocol-specified safety follow-up procedures to capture adverse events (AE), serious adverse events (SAE), and unanticipated problems (UPs).

Discontinuation from *Delaware* PEAK does not mean discontinuation from the study, and remaining study procedures should be completed as indicated by the study protocol. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Significant study intervention non-compliance
- If any clinical adverse event (AE), or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant

The reason for participant discontinuation or withdrawal from the study will be recorded. Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to respond to the 3-month follow-up and is unable to be contacted by the study site staff.

The following actions must be taken if a participant fails to respond to a required follow-up visit:

- The site will attempt to contact the participant and reschedule the missed visit and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary,

a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record or study file.

- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 EFFICACY ASSESSMENTS

Primary outcome measures (Physical Activity):

Participants will be sent two activity monitors to measure their physical activity: 1) Actigraph GT3X monitor to be worn over the right hip during waking hours, and 2) activPAL 4 monitor, to be worn at all times on the right thigh (but can be switched to the left thigh, if needed). Participants will be instructed to wear both monitors for 7 consecutive days, and then return the monitors via mail in a pre-addressed, pre-stamped envelope that is provided.

As a secondary measure of physical activity, the International Physical Activity Questionnaire (IPAQ) will be given to study participants.

Secondary outcome measures (Health Beliefs and Self-efficacy):

- **Treatment Beliefs of OA (TOA) Physical Therapy:** A 9-item questionnaire that assesses health beliefs (positive and negative) related to physical therapy. This questionnaire takes approximately 5 minutes to complete.
- **TOA Physical Exercise:** A 13-item questionnaire that assesses health beliefs (positive and negative) related to physical activity. This questionnaire takes approximately 5 minutes to complete.
- **Self-efficacy for Exercise (SEE):** A 9-item questionnaire that assesses confidence (e.g., self-efficacy) in being able to exercise. This questionnaire takes approximately 5 minutes to complete.

Additional outcome measures:

The following clinical measures will also be collected:

- **Charlson Comorbidity Index (CCI):** A 17-item questionnaire that creates a weighted score based on a range of common, comorbid conditions. This questionnaire takes approximately 5 minutes to complete.
- **Visual Analog Scale (VAS) for pain:** A single-item questionnaire in which the participant makes a mark on a 100 mm line to indicate their pain score in each knee from 0-100. This questionnaire takes <1 minute to complete.
- **Knee Injury and Osteoarthritis Outcome Score (KOOS):** A 42-item questionnaire that assesses the following five domains: pain, symptoms (other than pain), function in activities of daily living, function in sport and recreation, and quality of life. This questionnaire takes approximately 10 minutes to complete.
- **Test of Knowledge about Knee OA:** A 5-item instrument used to assess OA knowledge. This instrument takes approximately 2 minutes to complete.

- **Treatment Expectations Question:** A single question of the study subject's expectations that the intervention they will receive will be effective for their knee.
- **Strengthening Exercise and Step Goal Adherence:** For the Expanded Intervention, adherence to strengthening exercises and physical activity will be measured by reviewing each participant's Red PEAK Knee Plan & Log Book and electronic records from the Fitbit™ monitor. A previous study shows that the use of a patient-reported log to record exercises is a valid method to measure adherence to a daily intervention. The participant will be classified as adherent to their strengthening exercises if > 50% of exercises were completed as prescribed. The participant will be classified as adherent to their step goals if the goal was met or exceeded on > 50% of days. This benchmark is based on a previous intervention study where adherence ranged from 45-60%. Adherence to the Expanded Intervention will be measured at the 12-week follow-up timepoint. We hypothesize (H3a) that participants will meet $\geq 50\%$ of assigned exercise and physical activity goals. For the Brief Intervention, adherence will be measured via a self-report questionnaire administered on REDCap. The participant will be asked to confirm that they viewed the informational video, accessed the associated weblink, and note how many times they visited the site for each webpage section. Adherence to the Brief Intervention will be measured at the 12-week follow-up timepoint.
- **Telehealth Acceptability:** Acceptability of the Expanded Intervention will be measured with the Telehealth Acceptability (TA) questionnaire. The TA is a 14-item questionnaire about their feelings towards telehealth and takes approximately 5 minutes to complete. The TA will be collected at the 12-week follow-up timepoint. We hypothesize (H3b) that $\geq 75\%$ of participants will find PEAK to be acceptable.
- **Participant Satisfaction:** Participant satisfaction with care received will be measured with the Participant Satisfaction form. The form contains the question, "How satisfied are you with the intervention that you received?", rated on a 7-point Likert scale ranging from "0: extremely unsatisfied" to "6: extremely satisfied" and three open-ended questions asking about the participant's experience with the intervention. Participant satisfaction will be collected at the 12-week follow-up timepoint. We hypothesize (H3c) that $\geq 75\%$ of participants will be satisfied with PEAK.
- **LPA, SED, Daily Walking:** Data collected using the Actigraph GT3x and the ActivPAL4 activity monitors will also be used to assess change in minutes per week of LPA, minutes per week of SED, and average steps per day between baseline and both follow-up timepoint. Additionally, change in minutes per week of MVPA between the baseline and 24-week follow-up timepoint will be assessed.
- **Test of Knowledge about Knee OA:** The participant will complete a Test of Knowledge about Knee OA, which is a 5-item questionnaire used to assess how much the participant knows about knee OA. The questionnaire takes approximately 5 minutes to complete and will be collected at the baseline timepoint.
- **Treatment Expectations Question:** The participant will complete a Treatment Expectations Question, which asks the participant how effective they expect the intervention to be for their knee. This question will be collected at the baseline timepoint.

8.2 SAFETY AND OTHER ASSESSMENTS

A research team member will call the individual via phone and verbally ask questions on the **Verbal Eligibility Form**, which will confirm their answers to the Screening Form questions, but will also ask about other study inclusion/exclusion criteria to ensure that they are eligible. Three outcomes can occur:

- First, the individual is ineligible for the study, in which case the participant will be notified by the research team member while on the call. All data collected through the Screening Form and the Verbal Eligibility Form will be de-identified and stored.
- Second, the individual is eligible for the study, but needs to obtain medical clearance from a physician to ensure they can safely participate in the study. We will require medical clearance if the individual reports a fall in the past 12 months (Question #13), is house-bound due to immobility (Question #14), or answers “yes” to any item from Stage 1 of the **Adult Pre-Exercise Screening System** (APSS) questionnaire (Questions #15-20). After obtaining medical clearance, participants must verbally confirm they have received medical clearance with a research team member, which will be documented.
- Third, the individual is eligible for the study and does not need medical clearance for any of the reasons listed above.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

We define an AE as any unfavorable medical occurrence temporally associated with the study, including any abnormal symptom or disease, regardless if it is related to participation in the research.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

We define an SAE as any undesirable experience in a patient that results in death, is life-threatening, requires initial or prolonged hospitalization, or results in persistent or significant disability. We applied definitions of an Adverse Event (AE) and Serious Adverse Event (SAE) consistent with the IRB and FDA.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

The following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant’s daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant’s usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

All adverse events (AEs) must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study intervention administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study intervention (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.
- **Potentially Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, other factors may have contributed to the event (e.g., the participant’s clinical condition, other concomitant events). Although an AE may rate only as “possibly related” soon after discovery, it can be flagged as requiring more information and later be upgraded to “probably related” or “definitely related”, as appropriate.
- **Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study intervention administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study intervention) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant’s clinical condition, other concomitant treatments).
- **Not Related** – The AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.]

8.3.3.3 EXPECTEDNESS

The Executive Team will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The research assistant will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.3.5 ADVERSE EVENT REPORTING

Any AE is to be recorded by the Research Team using forms provided by the University of Delaware Institutional Review Board and Research Office. In order to avoid vague, ambiguous, or colloquial expressions, the AE will be recorded in standard medical terminology rather than the patient's own words. Whenever possible, the investigator will combine signs and symptoms that constitute a single diagnosis.

The study team may become aware of an AE through spontaneous report of the patient (e.g., via phone call or email), or through scheduled intervention consultations for participants in the Expanded intervention group. The reporting period begins at the time of study enrollment and lasts through the 12-week follow-up data collection. Any events will be followed until resolution or until the participant completes the study, whichever comes first.

Each AE is to be evaluated for duration, severity, seriousness, and causal relationship to the intervention. The action taken and the outcome must also be recorded.

Unexpected serious suspected adverse reactions are subject to expedited reporting to the IRB. relationship to the intervention at the time of the initial report.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

A research assistant will immediately report to the sponsor any serious adverse event, whether or not considered study intervention related, including those listed in the protocol or investigator brochure and must include an assessment of whether there is a reasonable possibility that the study intervention caused the event. Study endpoints that are serious adverse events (e.g., all-cause mortality) must be reported in accordance with the protocol unless there is evidence suggesting a causal relationship between the study intervention and the event (e.g., death from anaphylaxis). In that case, the investigator must immediately report the event to the sponsor.

All serious adverse events (SAEs) will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the participant is stable. Other supporting documentation of the event may be requested by the Data Coordinating Center (DCC)/study sponsor and should be provided as soon as possible.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

Include content in this section if applicable, otherwise note as not-applicable.

AEs and SAEs, and study-related results will be reported to study participants on an aggregate level.

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

<Insert text>

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS (UP)

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research (“possibly related” means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEM REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the Data Coordinating Center (DCC)/lead principal investigator (PI). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB and to the DCC/study sponsor within <insert timeline in accordance with policy> of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and to the DCC/study sponsor within <insert timeline in accordance with policy> of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within <insert timeline in accordance with policy> of the IRB's receipt of the report of the problem from the investigator.]

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Participants will be informed about UPs on an aggregate level.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

State the formal and testable null and alternative hypotheses for primary and key secondary endpoints, specifying the type of comparison (e.g., superiority, equivalence or non-inferiority, dose response) and time period for which each endpoint will be analyzed.

- Primary Efficacy Endpoint(s):

Our primary study endpoint will be change in moderate-to-vigorous intensity physical activity (MVPA) from baseline to 12 weeks. We hypothesize that the expanded intervention group will have greater change in MVPA compared with the brief intervention group.

- Secondary Efficacy Endpoint(s):

Our secondary study endpoints are change in 1) Health Beliefs and 2) Self-Efficacy for Exercise from baseline to 12 weeks. We hypothesize that the expanded intervention group will have greater change in Health Beliefs and Self-Efficacy compared with the brief intervention group. Additionally, our secondary study endpoint will be change in moderate-to-vigorous intensity physical activity (MVPA) from baseline to 24 weeks.

9.2 SAMPLE SIZE DETERMINATION

Sample size was determined by powering our primary study outcome. For the mixed design ANOVA models (H1a, and H2) this study will be adequately powered (power ≥ 0.80) with 84 participants, 42 in each group, for detecting a moderately small interaction effect ($d=0.30$), i.e. the difference from pre to post between groups, with a moderate correlation among repeated measures ($r=0.50$) and type I error = 0.05. We will recruit 100 participants to account for an estimated loss to follow up of 15%.

9.3 POPULATIONS FOR ANALYSES

We will use an Intention-to-Treat (ITT) analysis using Mixed Models to avoid listwise deletion. As well, we will conduct a Per-Protocol Analysis restricting our dataset to only those who completed the study and attended at least 4 of the 5 consultation sessions.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Demographic summary information about the sample will be presented using means and standard deviations for continuous measures, and frequencies and percentages for categorical data. We will also inspect if groups are balanced after randomization by comparing subject characteristics between groups using t-tests and χ^2 tests. If a subject characteristic is different between groups, it will be included as a covariate to adjust for potential confounding. All analyses will be performed as per protocol and intention to treat to assure that missing data do not impact results. All analyses will use nominal alpha, set to 0.05.

9.4.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

Our primary outcome is change in MVPA from baseline to 12 weeks, which is a continuous outcome. MVPA is measured from the Actigraph monitor and in units of minutes/day. We will use 2 x 2 Mixed Design ANOVAs, to test if the change over time in outcomes is different between groups. These models assume linearity, Sphericity, Homogeneity of Covariance Matrices, and normality, which will be evaluated using Box-Cox, Mauchly's, Box's M, and Shapiro-Wilk tests, respectively. Outliers and influential cases will be screened for and removed.

If the assumptions are violated and cannot be satisfied by transformations suggested by the Box-Cox test, then Generalized Linear Modeling will be employed. As a secondary analysis, we will adjust the model for potential confounders, including age, sex, and BMI. We will conduct an ITT analysis and a per-protocol analysis.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Our second outcomes are 1) MVPA from baseline to 24 weeks, 2) change in health beliefs from baseline to 12 weeks and 3) change in self efficacy from baseline to 12 weeks. All these secondary outcomes are continuous. We will use 2 x 2 Mixed Design ANOVAs, to test if the change over time in outcomes is different between groups. These models assume linearity, Sphericity, Homogeneity of Covariance Matrices, and normality, which will be evaluated using Box-Cox, Mauchly's, Box's M, and Shapiro-Wilk tests, respectively. Outliers and influential cases will be screened for and removed. If the assumptions are violated and cannot be satisfied by transformations suggested by the Box-Cox test, then Generalized Linear Modeling will be employed. As a secondary analysis, we will adjust the model for potential confounders, including age, sex, and BMI. We will conduct an ITT analysis and a per-protocol analysis.

9.4.4 SAFETY ANALYSES

Safety endpoints will be analyzed as summary statistics. We will not be formally evaluating a safety endpoint.

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Not applicable

9.4.6 PLANNED INTERIM ANALYSES

Not applicable

9.4.7 SUB-GROUP ANALYSES

For all analyses, we will conduct an exploratory analysis stratifying our data by sex, to examine sex-specific effects.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will not be listed.

9.4.9 EXPLORATORY ANALYSES

Not applicable

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

No text is to be entered in this section; rather it should be included under the relevant subheadings below.

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

No text is to be entered in this section; rather it should be included under the relevant subheadings below.

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention. The following consent materials are submitted with this protocol '1. PEAK Informed Consent.pdf'

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. This process will take place remotely. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be emailed to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, and the funding agency. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, and/or IRB.

Participant Termination Criteria:

If a participant does not wear the activity monitors (Actigraph and activPAL) for at least 4 days in the 2-week period allotted, they will be terminated from the study. The treating physical therapist may also recommend termination of participants if there are concerns about their safety during the expanded intervention, for example: unsafe demonstration of exercises, despite continued visual and auditory feedback from the therapist, and/or the emergence of an unexpected medical condition, which requires in-person attention. The PI will review these concerns and make the final decision regarding participant termination.

Should the subject be terminated, the participant will be encouraged to contact his/her current medical provider and the study team will offer to write a letter detailing the clinical concern to the participant's medical provider listed in the **Provider Form**.

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), regulatory agencies or pharmaceutical company supplying study product may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the Delaware ACTIVE Lab server. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management

systems used by clinical sites and by the Delaware ACTIVE Lab research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the Delaware ACTIVE Lab server.

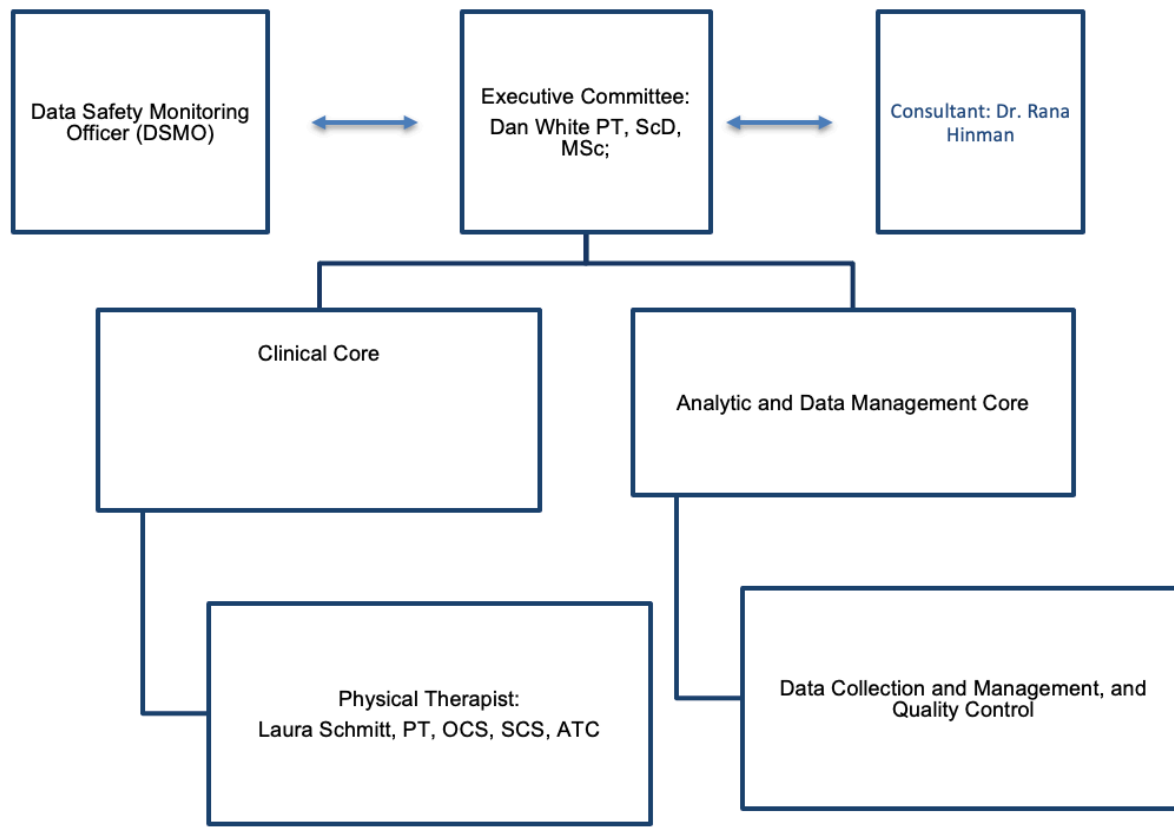
10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at the Delaware ACTIVE Lab server. After the study is completed, the de-identified, archived data will be transmitted to and stored at the Delaware ACTIVE Lab server for use by other researchers including those outside of the study. Permission to transmit data to the Delaware ACTIVE Lab server will be included in the informed consent.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Provide the name and contact information of the Principal Investigator and the Medical Monitor.

Principal Investigator	Medical Monitor
<i>Daniel K White PT, ScD</i>	<i>Karin Silbernagel, PT, PhD</i>
<i>University of Delaware</i>	<i>University of Delaware</i>
<i>540 S. College Dr. Newark DE</i>	<i>540 S. College Dr. Newark DE</i>
<i>302-831-7607</i>	<i>302-831-4808</i>
<i>dkw@udel.edu</i>	<i>kgs@udel.edu</i>

Study Organizational Structure**10.1.6 SAFETY OVERSIGHT**

Study oversight will be under the direction of a Data and Safety Monitoring Officer (DSMB) from an individual with the appropriate expertise, including rehabilitation, telehealth, and orthopedics. The Safety officer (SO) should be independent from the study conduct and free of conflict of interest, or measures should be in place to minimize perceived conflict of interest. The SO will review study records at least semiannually to assess safety and efficacy data on each arm of the study. The SO will operate under the rules of an approved charter.

10.1.7 CLINICAL MONITORING

Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with International Conference on Harmonisation Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

- Monitoring for this study will be performed by a research assistant.
- *Remote review of study records will occur every 6 months for a random review of certain data.*
- The research assistant will be provided copies of monitoring reports within 7 days of visit.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Each clinical site will perform internal quality management of study conduct, data and biological specimen collection, documentation and completion. An individualized quality management plan will be developed to describe a site's quality management.

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the clinical trial is conducted and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant enrolled in the study. Data recorded in the electronic case report form (eCRF) derived from source documents should be consistent with the data recorded on the source documents.

Clinical data (including adverse events (AEs), concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into <specify name of data capture system>, a 21 CFR Part 11-compliant data capture system provided by the <specify Data Coordinating Center>. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

<Insert text>

10.1.9.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 2 years after the last approval of a marketing application in an International Conference on Harmonisation (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

<Insert text>

10.1.10 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, section 5.1.1
- 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 14 working days of identification of the protocol deviation, or within 7 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive [PubMed Central](#) upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers x years after the completion of the primary endpoint by contacting <specify person or awardee institution, or name of data repository>.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the <specify NIH Institute or Center (IC)> has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS

The list below includes abbreviations utilized in this template. However, this list should be customized for each protocol (i.e., abbreviations not used should be removed and new abbreviations used should be added to this list).

AE	Adverse Event
ANCOVA	Analysis of Covariance
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FFR	Federal Financial Report
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ISO	International Organization for Standardization
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
MSDS	Material Safety Data Sheet
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee

SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A Summary of Changes table for the current amendment is located in the Protocol Title Page.

[illegible]

11 REFERENCES

Include a list of relevant literature and citations for all publications referenced in the text of the protocol. Use a consistent, standard, modern format, which might be dependent upon the required format for the anticipated journal for publication (e.g., N Engl J Med, JAMA, etc.). The preferred format is International Committee of Medical Journal Editors (ICMJE). Include citations to product information such as manufacturer's IB, package insert, and device labeling.

Examples:

- **Journal citation**
Veronesi U, Maisonneuve P, Decensi A. Tamoxifen: an enduring star. J Natl Cancer Inst. 2007 Feb 21;99(4):258-60.
- **Whole book citation**
Belitz HD, Grosch W, Schieberle P. Food chemistry. 3rd rev. ed. Burghagen MM, translator. Berlin: Springer; 2004. 1070 p.
- **Chapter in a book citation**
Riffenburgh RH. Statistics in medicine. 2nd ed. Amsterdam (Netherlands): Elsevier Academic Press; c2006. Chapter 24, Regression and correlation methods; p. 447-86.
- **Web Site citation**
Complementary/Integrative Medicine [Internet]. Houston: University of Texas, M.D. Anderson Cancer Center; c2007 [cited 2007 Feb 21]. Available from: <http://www.manderson.org/departments/CIMER/>.
- **Electronic Mail citation**
Backus, Joyce. Physician Internet search behavior: detailed study [Internet]. Message to: Karen Patrias. 2007 Mar 27 [cited 2007 Mar 28]. [2 paragraphs]
- **References to package insert, device labeling or investigational brochure**
Cite date accessed, version number, and source of product information.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY**Title:** Physical Exercise and Activity for Knee osteoarthritis (PEAK)**Principal Investigator:** Daniel K White, PT, ScD, MSc**KEY INFORMATION**

Important aspects of the study you should know about first:

- **Purpose:** The objective of this study is to study how a brief versus expanded exercise and physical activity program, each delivered online, may increase physical activity in adults with knee osteoarthritis (OA).
- **Procedures:** If you choose to participate, you will be asked to answer questionnaires about your health and wear two activity monitors (one on your thigh and the other around your waist) for 7 days. You will be assigned to participate in either one (Brief) or five (Expanded) online sessions that review exercise and physical activity for knee OA. If you are assigned to receive five (Expanded) online sessions, you will also be asked to perform exercises for 10-20 minutes/day repeated 3 to 5 days/week, while step goals will take 20 to 30 minutes/day every day of the week.
- **Duration:** This study lasts about 6 months.
- **Risks:** There are minimal risks to participating in this study, namely muscle soreness from increased activity, and a risk of loss of confidentiality.
- **Benefits:** You may experience a relief in knee pain, an increase in muscular strength, and an improvement in your physical activity.
- **Alternatives:** If you choose to enroll in this study, we ask that you do not seek in-person Physical Therapy for your knee OA for the duration of the study. However, as an alternative, you can choose not to enroll in the study and seek in-person Physical Therapy for your OA.
- **Costs and Compensation:** If you decide to participate in this study, there is no cost to you. If you complete this study, you will be compensated with \$50 in Amazon Gift cards.
- **Participation:** Taking part or not in this research study is your decision. You can decide to participate and then change your mind at any point.

Please carefully read the entire document. You will have the opportunity to ask any questions you may have before deciding if you want to participate.

You are being invited to participate in a research study. This consent form tells you about the study including its purpose, what you will be asked to do if you decide to take part, and the risks and benefits of being in the study. Please read the information below and ask us any questions you may have before you decide whether or not you want to participate.

PURPOSE OF THE STUDY

A physical therapist can help adults with knee osteoarthritis (OA) manage their knee problems. Physical Therapy (PT) typically includes a structured exercise program with advice about how to manage and increase physical activity levels. We would like to evaluate how an exercise program with advice about OA management may be delivered online to adults with knee OA.

This study will compare two different online programs for adults with knee OA. Both programs will review strengthening exercises, physical activity goals, and resources to help manage pain associated with knee OA. Again, both programs take place online and do not require that you leave your home.

The first program is a brief program, which includes an online, guided video orientation from a physical therapist to web resources for strengthening exercises, physical activity, and pain management strategies for knee OA. The second program is an expanded program, which includes 5 online consultations with a physical therapist over a 12-week period who will prescribe strengthening exercises, physical activity goals, and pain management strategies for knee OA. We will collect measures about your health when you start either program, 12 weeks after you start, and 24 weeks after you start.

WHO IS BEING ASKED TO PARTICIPATE?

You can safely participate in the study if you meet the following criteria:

- You reside in the contiguous United States (48 states, excluding Hawaii and Alaska)
- You are comfortable participating in a program delivered in English
- You are at least 45 years old
- You are interested in becoming more physically active
- You have activity-related knee pain that has not already been addressed by a knee replacement
- You have no morning knee stiffness, or morning stiffness that lasts less than 30 minutes
- You have a device with an internet connection and a working email address
- You do not require medical clearance to increase your physical activity, or you have obtained medical clearance to increase your physical activity
- You are willing to wear activity monitors for 7 days in the next 2 weeks, and participate in online sessions and data collection over 12 weeks

There are also certain criteria that may indicate this study is not suitable for you:

- You are scheduled for a knee replacement in one or both knees
- You already exercise more than 60 minutes/week of moderate-to-vigorous intensity physical activity
- You have participated in a supervised and formal strength training program for your leg muscles in the past 6 months
- You have had Physical Therapy for your knee OA in the past 6 months

- You are unable or unwilling to obtain medical clearance to increase your physical activity after it was determined that you require medical clearance

PROCEDURES: WHAT WILL YOU BE ASKED TO DO?

Step 1: Answering Questionnaires and Wearing the Activity Monitors at Baseline

You will be asked to answer questionnaires to provide us with general information about yourself, as well as information about your knee pain, difficulties with daily tasks, previous/current strategies used to manage your knee OA, and your expectations for this study. Answering the questionnaires can take some time (up to 60 minutes) and may seem repetitive, but every question is there for a reason and all the information you give to us is valuable. If you are not comfortable completing the surveys online, you can request paper copies of the surveys to be mailed to you along with a prepaid envelope to return the forms to us. We will also ask for contact information for your primary care provider and/or orthopedic specialist - this will only be used if any concerns arise regarding your participation in this study.



We will also ask you to wear two activity monitors: the Actigraph GT3X (left, worn on the hip) and the activPAL 4 (right, worn on the thigh). Together, these monitors can accurately measure your walking, sitting, and standing behaviors. We ask that you wear both monitors for 7 consecutive days, as this is needed for a valid estimate of your physical activity. You will receive a form that provides additional instructions for wearing the monitors. You will also receive a text reminder to wear the monitors. You will be given up to 2 weeks to wear them; if you do not wear both monitors for at least 4 days, you will not be allowed to continue with the study.

Step 2: Random Assignment to, and Participation in, a Brief or Expanded Online Program for Knee OA

After you complete the questionnaires and wear the monitors, a research assistant will tell you which group you are randomly assigned to: 1) the Brief Online Program or 2) the Expanded Online Program.

If you are assigned to the Brief Online Program, you will be emailed a link to a website and you will be guided by a PT. You can review the website at your own pace. This site has links to OA-specific resources to start a strengthening program, increase your physical activity by walking, tips for managing knee pain, and a helpline to contact for specific questions. A physical therapist will orient you to these resources via a several short, pre-recorded videos. We may ask you how many times you access these resources.

If you are assigned to the Expanded Online Program, the research assistant will ask you to schedule five online consultations that are convenient for you and based on the Physical Therapist's availability. These consultations will be hosted on a secure, video-conferencing software that can be used on a computer, tablet, or smartphone. The first consultation (Week 0) will last around 60 min, and will be followed by 4

consultations at Weeks 2, 4, 7, 10, each lasting around 45 min. You will receive text reminders before each session. You will receive a Welcome Letter, four resistance bands for exercising, an activity tracker that provides you with feedback regarding your physical activity, and instructions for using the activity tracker. Exercises are estimated to take between 10 to 20 minutes/day repeated 3 to 5 days/week, while step goals will take 20 to 30 minutes/day every day of the week. You will be expected to perform prescribed exercises on your own time. The Physical Therapist will record brief notes from each consultation, and the consultations will be video and audio recorded for use only by the research team. Recordings (audio + video) of the 5 consultations will be stored as password-protected files on a secure server. Recordings will be electronically stored for 1 year after the study ends. The recordings will be used for future educational purposes, and only study team members will have access to the recordings. Your identity will be kept confidential. Please note, your identity will not be revealed in any reports or publications related to the study. We will ask for a phone number of a friend or family member who is able to reach you should you need assistance during any of the consultations. We will also ask you for your location during each consultation in case Emergency Services must be used. At the conclusion of the study, we may create a map that displays the counties that participants live in, but your county will not be linked to your name.

You will also be asked to authorize the research team to access, view, and download data from your activity tracker through a secure research platform called Fitabase. Fitabase is an online system that can remotely collect and store data from your activity tracker. We will create an email address and password for you and set up a Fitbit® account for you. You will be asked to 1) link your Fitbit® account to the secure platform (Fitabase), and 2) authorize the research team to view your data. However, your data will be given a unique study identifier so that your name and other personal information remain confidential. Your Fitbit username and password will not be accessed, viewed, or stored by Fitabase or the research team. When you authorize Fitabase to access and store your data, you are agreeing to the Terms of Use and Privacy Policy set by Fitabase. You will be able to review the Terms of Use and Privacy Policy prior to authorization, and may request a hard copy from the research team if desired.

Step 3: Answering Questionnaires and Wearing the Activity Monitors at 12 weeks and 24 weeks

One week before each follow-up visit (that is, 11 weeks and 23 weeks after you start the intervention), you will be contacted and asked about any injuries or surgeries since your last contact with the research team. You will also be asked to answer a brief questionnaire.

Then, at each follow-up visit (12 weeks and 24 weeks), you will again be asked to answer questionnaires to provide us with information about your knee pain, difficulties with daily tasks, previous/current strategies used to manage your knee OA, and your expectations for this study. Answering the questionnaires can take some time (up to 45 minutes) and may seem repetitive, but every question is there for a reason and all the information you give to us is valuable. If you are not comfortable completing the surveys online, you can request paper copies of the surveys to be mailed to you along with a prepaid envelope to return the forms to us.

We will also ask you to again wear two activity monitors: the Actigraph GT3X (left, worn on the hip) and the activPAL 4 (right, worn on the thigh). Together, these monitors can accurately measure your walking,

sitting, and standing behaviors. We ask that you wear both monitors for 7 consecutive days, as this is needed for a valid estimate of your physical activity. You will receive a form that provides additional instructions for wearing the monitors.

WHAT ARE POSSIBLE RISKS AND DISCOMFORTS?

There are some risks associated with participation in this study, which have been listed below. However, we will take every precaution to reduce these risks.

- There are risks associated with participation in an exercise program. There is a minimal risk of an adverse medical event, i.e., an unexpected event such as ill health, physical harm, or death. Much more common are risks associated with participation typically found during physical therapy, e.g., risk of soreness from exercises designed to increase muscle strength or length, fluctuating knee pain and/or swelling related to knee OA, and fatigue during or following the treatment. There is a minimal risk of a loss of balance during exercises that involve standing or single limb stance. There is a minimal risk for starting a supervised physical activity program, including a mild temporary increase in knee pain. There are no known risks associated with receiving education on web-based resources for strengthening and physical activity. Should you initiate exercise, there is risk of muscular soreness, fluctuating knee pain and/or swelling related to knee OA, and fatigue during or following exercise. Should the participant start the 'Walk with Ease' program, there is risk of a mild, temporary increase in knee pain. If you experience any problems, you should notify the research team and/or the Physical Therapist during your consultations.
- Some of the questionnaires you will be asked to complete require you to consider your pain, how this pain affects your daily tasks, and other health problems you may have. It is possible that some people could find these questions difficult emotionally, although we have not found this to be a problem in other similar studies.
- The thigh-worn activity monitor is adhered to the skin using a Tegaderm dressing, which may cause minor skin irritation. To avoid this, you may periodically switch the thigh-worn monitor to your other thigh.
- There is a possibility of a breach of confidentiality if data or identifying information should accidentally be released; however, we will make every effort to ensure that data is stored securely in a manner that maintains your confidentiality.

WHAT ARE POTENTIAL BENEFITS FROM THE STUDY?

You may experience relief of your knee OA symptoms (pain, stiffness, etc.) and an increase in your lower body strength. You may also increase your physical activity, which lowers your risk of poor future health, such as lowering the risk of diabetes, cardiovascular disease, and premature mortality.

NEW FINDINGS THAT COULD AFFECT YOUR PARTICIPATION

During the course of this study, we may learn new important information. This may include information that could cause you to change your mind about participating in the study. If any new important information becomes available while you are a participant, we will let you know.

CONFIDENTIALITY: WHO MAY KNOW THAT YOU PARTICIPATED IN THIS RESEARCH?

Your study data will be handled as confidentially as possible. If results of this study are published or presented, individual names and other personally identifiable information will not be used.

To minimize the risks to confidentiality, we will link each participant name to a **participant identification (ID) number**. This number will replace your name on all questionnaires and activity data.

We will store the list that links each participant's name to their ID number on a secure server with password protection, which is accessible only to the research team.

The research team will make every effort to keep all research records that identify you confidential. The findings of this research may be presented or published. If this happens, no information that gives your name or other details will be shared.

We will keep your study data as confidential as possible, with the exception of certain information that we must report for legal or ethical reasons, such as child abuse or any intent to hurt yourself or others. If required, your records may be inspected by authorized personnel in the University of Delaware Institutional Review Board.

Your identity will remain protected for all video and audio recordings, as only professional audiences or health professionals in training authorized by the study team will be able to view recordings. Recordings will be kept indefinitely.

USE OF DATA COLLECTED FROM YOU IN FUTURE RESEARCH:

All data collected as part of the study will not be used or distributed for future research studies even after identifiers are removed.

COSTS AND COMPENSATION

There are **no** costs associated with participating in the study.

You will be compensated with a \$25 Amazon Gift Card after you return all activity monitors at 12 weeks. You will be compensated with another \$25 Amazon Gift Card after you complete the study and return all activity monitors, as well as the feedback monitor (if you received the Expanded Online Program) at 24 weeks.

WHAT IF YOU ARE INJURED DURING PARTICIPATION IN THE STUDY?

If you are injured while participating in the study, you can contact the research team at the University of Delaware at any time via phone call or email. If you need additional medical treatment, the cost of this treatment will be your responsibility or that of a third-party payer (for example, your health insurance). By signing this document, you are not waiving any rights that you may have if injury was the result of negligence of the university or its investigators.

DO YOU HAVE TO TAKE PART IN THIS STUDY?

Taking part in this research study is your decision. You do not have to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide later not to participate, or if you decide to stop taking part in the research, there will be no penalty or loss of benefits to which you are otherwise entitled.

Your decision to stop participation, or not to participate, will not influence current or future relationships with the University of Delaware.

The investigators reserve the right to remove you from the study without your consent at such time that they feel it is in your best interest.

If you decide to withdraw from the study, please inform our research team. We will keep any data collected from you up until that point. We will not contact you further regarding the study.

INSTITUTIONAL REVIEW BOARD

This research study has been reviewed and approved by the University of Delaware Institutional Review Board (UD IRB), which is a committee formally designated to approve, monitor, and review biomedical and behavioral research involving humans. If you have any questions or concerns about your rights as a research participant, you may contact the UD IRB at hsrb-research@udel.edu or (302) 831-2137.

CONTACT INFORMATION

If you have any questions about the purpose, procedures, or any other issues related to this research study you may contact the Principal Investigator, **Daniel K. White**, at 302-831-7607 or dkw@udel.edu.

In the case of any unfavorable medical events that occur while you are a participant in the study, please contact **Jennifer Copson**, at 302-317-1122 or peak-study@udel.edu.

CONSENT TO PARTICIPATE IN THE RESEARCH STUDY:

I have read and understood the information in this form and I agree to participate in the study. I am 18 years of age or older. I have been given the opportunity to ask any questions I had and those questions have been answered to my satisfaction. I understand that I will be given a copy of this form for my records.

Printed Name of Participant
(PRINTED NAME)

Signature of Participant
(SIGNATURE)

Date

Person Obtaining Consent
(PRINTED NAME)

Person Obtaining Consent
(SIGNATURE)

Date

OPTIONAL CONSENT TO BE CONTACTED FOR FUTURE STUDIES:

Do we have your permission to contact you regarding participation in future studies? If you agree to being contacted in the future, we will keep your contact information. Please write your initials next to your preferred choice.

_____ YES

_____ NO